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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/981,087	05/27/98	ELMORE M	1581.0200000

HM12/0605

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EXAMINER	
TURNER, S	
ART UNIT	PAPER NUMBER
1647	19

DATE MAILED: 06/05/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/981,087	Elmore et al
Examiner	**Art Unit**
Sharon L. Turner, Ph.D.	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 6-16-00, 6-19-00, 3-27-01

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 3-28 and 30-33 is/are pending in the applica

4a) Of the above, claim(s) 13-18 and 25 is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 3-12, 19-24, 26-28, and 30-33 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

Response to Amendment

1. The Examiner of U.S. Patent application SN 08/981,087 has changed. In order to expedite the correlation of papers with the application please direct all future correspondence to Examiner Turner, Technology Center 1600, Art Unit 1647.

2. Claims 3-28 and 30-33 are pending.

3. As a result of applicants amendments filed 6-16-00, 7-19-00 and 3-27-01, all rejections not reiterated herein have been withdrawn by the examiner.

Rejections Maintained

4. Claims 13-18 and 25 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. This application contains claims 13-18 and 25 drawn to an invention nonelected with traverse in Paper Nos. 7, 12 and 13. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

6. It is noted that Applicants Petition under Rule 181 filed Jan 7, 2000 is of record in the file and that the response has yet to be received by applicant. Should the response not follow this Office Action in a timely fashion applicant is urged to contact either the Examiner or SPE Gary Kunz to further expedite the response.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Cancelled

8. Claims 22-24 stand rejected under 35 U.S.C. 112, first paragraph, as set forth in Paper No. 14, mailed 3-16-00 because the specification, while being enabling for increased survival against challenge with C. botulinum Langland BoNT/F by immunization with MBP-BoNT/$F_{848-1278}$ fusion protein, does not reasonably provide enablement for claims 22-24 as claimed in particular with respect to any protein which is free of botulinum activity, free of toxoid and with respect to protection against type F botulinum toxin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants argue that in contrast to the examiner's interpretation, Jobling et al., published four years before the instant priority date supports the enablement of the claims because the skilled artisan would be able, given the structure and function of botulinum toxin, to make and test for those embodiments within the scope of the claims.

Applicant's arguments filed 6-16-00 have been fully considered but they are not persuasive. The specification teaches but a single embodiment which provides benefit to animals upon immunization. This peptide constitutes the peptide sequence of residues 848-1278 of BoNT/F. However the claims encompass shorter peptide sequences which may or may not

retain those epitopes responsible for protection to the host, including survival upon challenge. Applicants suggest that the artisans ability to make and test for those variable sequences which provide for survival provides an enabling disclosure. However, the ability to make and test is not the standard of an enabling disclosure. In accordance with In re Wands, the accumulation of evidence must enable the skilled artisan the predictable ability to make and use the claimed invention. As pointed out in the previous Office action, the instant specification fails to identify any predictable measure of the claimed immunogenic fragments which retain protective activity. The skilled artisan recognizes the unpredictable nature of designating protein function based on divergent structure, even after the time of the invention, see in particular Skolnick et al., Trends in Biotech 18(1):34-39, 2000. Thus, in the absence of further guidance, the practitioner would be required to perform further undue experimentation to arrive at those fragments which retain immunological protective activity. The specification fails to disclose those residues which are required or are dispensable for the observed host effects. The standard for an enabling disclosure is not one of making and testing and the claims constitute a "wish to know". The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, those changes which can be made and still maintain immunological protection is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986).

New Rejections Necessitated by Amendment

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

10. Claims 3-4, 7-10, 12, 19-24, 26-27 and 30-33 are rejected as set forth in Paper Nos. 10, 14 and as set forth herein under 35 U.S.C. 102(a) as being anticipated by Sesardic et al (PCT Publication No. WO 94/21684, publication date 9/29/94) as evidenced by Sigma Catalog 1992, p. 1585 and 1592-93.

Applicants argue that the rejection appears to be over a single amino acid and that thus the claim amendments obviate the rejection, that the examiner does not point to where Sesardic teaches protection via an immunological response or how Sigma contributes to the rejection of claim 3.

Applicants arguments filed 6-16-00 have been fully considered but are not persuasive. Applicants are referred to the rejections of record in Paper Nos 10 and 14. As previously set forth peptide P1 of Sesardic Table 1, p. 12 meets the limitations of applicants claims and is more than a single amino acid. Sesardic was not deficient as interpreted by the examiner. The rejections were set forth separately only as the previous rejection of Sesardic was maintained as previously set forth in Paper No. 10. The rejection of the above claims are maintained over Sesardic as set forth in Papers No. 10 and 14. The Sigma catalog supports that any amino acid

may aid in the purification of a peptide by affinity (column) chromatography as specifically claimed in claims 9-10 but are also relevant to the recitation of peptides capable of enhancing or facilitating purification of the composition. The benefits with respect to immunity were previously noted for example at p. 18-20 and Tables 5-6. However, it is noted that the subject of the claims are the peptides. Any peptide which meets the structural limitations of the claims inherently provides for the recited functional characteristics of eliciting in a mammal an immunological response that is protective against type F botulinum toxin. It is not required that the reference teach such as such is not a limitation of the peptides per se, i.e., the recitation does not further limit the peptides themselves. Arguments to the contrary would necessarily preclude such claim rejections as set forth above for claims 22-24 which do involve administration and evaluation of such characteristics to the host mammal. The newly submitted claims are anticipated as the peptides correspond to fusions of the claimed sequences and are administered to a mammal.

11. Claims 1-4, 7-12 and 19-24, 26-27 and 30-33 are rejected under 35 U.S.C. 102(b) as set forth in Paper No. 14, mailed 3-16-00 and as set forth herein as being anticipated by Simon et al, US Patent No. 5,178,859, issued Jan. 12, 1993.

Applicants argue that Simon fails to teach the peptides that elicit immunological responses protective against type F botulinum toxin or methods of production or use of the same and fail to teach the structural requirements of the claims which require a polypeptide comprising a fragment or a derivative of a heavy chain of a type F botulinum neurotoxin.

Applicants arguments filed 6-16-00 have been fully considered but are not persuasive. There are no structural requirements of the claims which Simon has not met as the peptides correspond to a fragment and derivative of a heavy chain of a type F botulinum neurotoxin. Only a single amino acid appears to be required, the rest are derivatives. The properties of eliciting an immunological response are inherent in the peptides. Alternatively such would appear to be an admission that the structural peptides were not enabled for the claimed function. It is further noted that the functional limitation does not appear to further limit the claimed peptides structurally and thus was not considered a limiting feature of the peptides. The newly submitted claims are anticipated as the peptides correspond to fusions of the claimed sequences and are administered to a mammal.

12. Claim 8 is objected to because of the following informalities: "that it protective" in line 5 is considered a typo and should be "that is protective". Appropriate correction is required.

13. Claims 1-4, 7-10, 12, 19-24, 26-27 and 30-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Thompson et al., FEMS Microbiol. Letters, 108:175-82, 1993.

Thompson et al., teach isolated clones which correspond to various regions of BoNT/F. The clones are represented in Figure 1 and were expressed and total cell lysates isolated for all cloned toxin fragments for testing in the mouse bio-assay to confirm they were not toxic, see in particular p. 176, column 2, last paragraph. Table I also discloses variable homology in light and heavy chains among toxin sequences. The Thompson peptides share the fragment of instant SEQ ID NO:1, residues 198-219 corresponding to residues 1036-1057 of Thompson. Thus, the

isolated peptides would be expected to inherently correspond to the claimed peptides and provide for all protective immunogenic activities, absent evidence to the contrary.

14. Claims 3-12, 19-24, 26-28 and 30-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite peptides which correspond in structure to an amino acid sequence corresponding to a fragment or a derivative of a heavy chain of a type F botulinum neurotoxin. The claimed peptides are disclosed as providing when administered to a mammal the property of eliciting an immunological response that is protective against type F botulinum toxin. The peptide claims do not require administration and thus such property is deemed to be an inherent property of the peptides within the scope of the claim. The functional limitation is not deemed to further limit the structural properties of the claimed peptides. However, applicants arguments appear to maintain that certain peptides within the scope of the structural limitations do not provide such property and that the recitation further limits the peptides structurally to those peptides that do provide for the functional activity. Applicants are required in their subsequent response to clarify the metes and bounds of both the structural and functional limitations of the claims such that the examiner can properly determine the application of rejections with respect to 35 USC 112 and the prior art.

15. Claims 26-28 and 30-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 27 recites "the L chain and Hn epitopes of said *C. botulinum*" there is insufficient antecedent basis for such limitations in the claims and the skilled artisan cannot readily discern those peptides which are intended to be encompassed or excluded by such recitation. Clarification is required.

Status of Claims

16. No claims are allowed.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.
June 3, 2001

CHRISTINE J. SAOUD
PRIMARY EXAMINER

Christine J. Saoud